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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

WILSON, MICHAEL C

ART UNIT

PAPER NUMBER

1632

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33

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-------------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 08/889,355 | ENGLER ET AL. |
| | Examiner Michael C. Wilson | Art Unit 1632 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 06 February 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 41-53 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 41-53 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's arguments filed 5-16-01, paper number 20, have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 21, 22, 35, 36, 40, 54 and 55 have been canceled. Claims 40-53 remain pending and under consideration in the instant application. The effective filing date of the claimed invention remains July 8, 1997.

Specification

The abstract has been amended and is correct.

Claim Rejections - 35 USC § 112

1. Claims 40-53 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The specification teaches isolating Impurities I, II and III from BigCHAP; however, the specification does not describe their structure. Since the time of filing, the structure of Impurities I, II and III have been determined (see attached description provided in 09/112,074).

As a preliminary matter, applicants point out that the examiner had switched Impurity II and III in the previous office action. The Examiner agrees. The Examiner's understanding of the structure of Impurities II and III was based on drawings of Impurities II and III provided in a response in a related application (see paper attached to the office action of 4-23-02 describing Big CHAP and Impurities I-III), which are incorrect. Impurity II is in Fig. 22 and Impurity III is in Fig. 23 of 6,392,069.

Applicants agree BigCHAP and Impurity I do not correlate to the claims because they do not have the same tertiary nitrogen as Formula I (pg 4, 2nd para. of response).

Applicants state that in Impurity III, X1 is a saccharide group; therefore, Applicants agree that Impurity III does not correlate to Formula I (pg 4 , 3rd para. of response).

Applicants argue Impurity II correlates to Formulate I and is described in the specification as originally filed. Applicants' argument is not persuasive.

Applicants point to pg 3, line 15-21, for support of Formula I. The citation describes a compound having Formula I wherein:

X1 is cholic acid group or deoxycholic acid group; and X2 and X3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups; and wherein at least one of X2 and X3 is a saccharide group.

However, the citation merely reiterates claim 41 and does not describe any specific structure, namely Impurity II.

While Impurity II is a species within the genus of claim 41, the structure of Impurity II was not disclosed in this application. Nor is the structure readily apparent from the disclosure as originally filed. An adequate written description of Impurity II requires more than a mere description of the genus of the compound and a statement that Impurity II was isolated and part of the invention. What is required is a description of the structure of Impurity II itself. It is not sufficient to define a compound solely by its genus, i.e. claim 41, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of the specific structure of Impurity II and to identify other compounds within that genus. Also, describing a genus in the absence of knowledge as to the specific structure of one compound within the genus is not an

adequate description of that genus. Thus, claiming all compounds within the genus of claim 41 without describing the specific structure of one compound within the genus is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). In this case, the specification does not describe Impurity II as having two cholic acid groups (and not deoxycholic acid groups) as X1 and X2 or X3. It is not readily apparent from pg 3, line 15-21, that Impurity II has two cholic acid groups. The specification does not describe X2 or X3 as a pentose monosaccharide. Therefore, the structure of Impurity II is not readily apparent from pg 3 because the specific combination of elements in X1, X2 or X3 could not have been guessed.

Applicants argue Example 12 illustrates the procedure for making Impurity II (pg 5, last para.). Applicants' argument is not persuasive because the Example 12 does not describe the structure of Impurity II and because it is not readily apparent that Example 12 is synthesizing Impurity II. It is unclear that the process in Example 12 is specific to making Impurity II and not generic to making Impurities I, II or III or even BigCHAP. In context of the specification as a whole, it appears that applicants originally believed all of the Impurities were species of Formula I. However, as revealed in post-filing evidence, it was determined that only Impurity II was a species of Formula I. Thus, the structure of Impurity II is essential for one of skill to make a compound of Formula I as it is the only disclosed species specifically taught in the specification that fits within the genus claimed.

Applicants argue it is readily apparent that the "cholic acid group" claimed would have meant a derivative of cholic acid. Applicants point out that the cholic acid group is not deleted but substituted resulting in an amide bond. Applicants point to pg 9-11 of the response, which describes the synthetic procedure, and bond connectivity of Impurity II and Example 12 of the specification. Applicants' arguments are not persuasive. The specification does not describe the

bond connectivity of Impurity II as a substitution of the terminal CO₂H group resulting in an amide bond. The diagram on pg 11 of the response, describing the structure resulting from Example 12, is not present in the specification. Applicants' logic in numbering the carbons of the "cholic acid group" (pg 11) does not correlate to the claims. Carbon number 4 is a carboxyl group, which applicants argue is part of the "cholic acid group". However, the claim requires a carboxyl group plus a "cholic acid group" (having 4 carbons) for a total of 5 carbons. One of skill would not have known to label the carboxyl group attached to X1 in the claim as the fourth carbon of the "cholic acid group". The specification as originally filed did not teach Example 12 was the process used to make Impurity II. The synthesis process in Example 12 of the specification does not describe the resulting structure. As such, Example 12 merely invites one of skill to determine the structure of a compound that may or may not be part of the claim.

Applicants' argue they may be their own lexicographer and define a "cholic acid group" as a cholic acid without the terminal CO₂H (pg 7 of response). Applicants' argument is not persuasive. The specification does not define a "cholic acid group." The specification does not define a "cholic acid group" as a cholic acid without the terminal CO₂H, or in the instant case, as a substitution resulting in an amide bond.

Applicants state a person of skill in the art would have understood pg 9, line 8, in context of Example 12, described a cholic acid group as being a cholic acid with a substitution resulting in an amide bond. Applicants' argument is not persuasive. Example 12 does not teach Impurity II is the product being synthesized. Example 12 does not describe 3-aminopropyl-3'-N-gluconamidopropyl-amine as Impurity II. The specification does not describe the structure of cholic acid once it reacts with isobutylchloroformate in the presence of triethylamine. It is not clear that Example 12 is specific to making only Impurity II.

Applicants point to US Patents 5,856,202; 4,892,816; 4,458,015 which use the phrase "cholic acid group." Applicants' argument is not persuasive. None of the Patents describe

combining a carbon chain with a cholic acid side group causes the “substitution” of the terminal CO₂H cholic acid (i.e. a cholic acid without the terminal CO₂H) resulting in an amide bond.

Even if the structure of Impurity II was readily apparent in the specification as originally filed, the structure of Impurity II is not adequate written for all compounds having Formula I as claimed which encompasses numerous combinations of X₁, X₂ and X₃. These structures are significantly different and may have different functions than Impurity II. Therefore, Impurity II is not adequate to describe the genus claimed. The specification does not teach any compounds having a deoxycholic acid group, a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group. Thus, the specification does not adequately describe the genus claimed.

Applicants argue pg 3, lines 15-21, state the compounds may have a deoxycholic acid group, a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group. Applicants argue one species is disclosed. Therefore, applicants argue the specification provides adequate written description for the genus (pg 7-8 of response). Applicants' argument is not persuasive. The specification does not adequately describe the structure of Impurity II for reasons cited above; therefore, the specification does not describe one species of the genus. Assuming the specification did adequately describe the structure of Impurity II for argument's sake, applicants' argument would not be persuasive. Applicants do not provide any means of making or isolating compounds having such components. Pg 3, lines 15-21, is merely a wish to know compounds having such components and an invitation for further experimentation, which is not adequate written description of species within the genus.

Applicants describe the three carbons between the carbonyl carbon and the pentose ring (pg 9 of response). Applicants again point out that the terminal carbon of cholic acid is not deleted but substituted. Applicants' arguments are not persuasive. The synthetic scheme on pg 11 is not in the specification. The specification does not describe the substitution of the terminal carbon results in an amide bond.

Applicants describe the synthesis scheme for Impurity II (pg 12 of response). Applicants' argument is not persuasive. While one of skill may have known the structures of the compounds in Example 12, one of skill would have had no idea the resulting compound in Example 12 was Impurity II. One of skill would not have known the specific structure of the end product because the structure of the intermediate products and a description of the bi-products within the process are not disclosed. For example, pg 31, line 14, describes an intermediate product as a mixed anhydride. Pg 31, line 23, states pure fractions of a compound are isolated by column chromatography, but does not teach the structure of the compound.

Applicants mention Example 11 on pg 13 of the response. However, example 11 merely teaches isolating Impurities I, II and III and does not teach the structure of Impurity II. Example 11 does not teach Impurity II is 3-aminopropyl-3'-N-gluconamidopropyl-amine as described in Example 12.

In conclusion, the specification does not provide adequate written description for a compound having the structure of Formula I as claimed.

2. Claims 40-53 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Applicants argue pg 3, lines 15-21, and pg 9, lines 8-14, describe Impurity II as having two cholic acid groups and a pentose monosaccharide (para. bridging pg 13-14 and pg 15, Section C of response). Applicants' argument is not persuasive because the citations do not reference Impurity II and because the citations are generic to Formula I and do not specifically lead one of skill to the structure of Impurity II.

Applicants argue it is readily apparent that the "cholic acid group" claimed would have meant a derivative of cholic acid. Applicants point out that the cholic acid group is not deleted but substituted resulting in an amide bond (pg 14 of response). Applicants' arguments are not persuasive. The specification does not teach one of skill that Impurity II has two cholic acid groups, or has a substitution of the terminal CO₂H group of the cholic acids groups resulting in an amide bond. The specification does not teach the structure resulting from Example 12. The specification does not teach Example 12 was the process used to make Impurity II. The specification does not describe the structure resulting from Example 12. It is unclear that the process in Example 12 is specific to making Impurity II and not generic to making Impurities I, II or III or even BigCHAP. Applicants' logic in numbering the carbons of the "cholic acid group" (pg 11) does not correlate to the claims. Carbon number 4 is labeled a carboxyl group, which applicants argue is part of the "cholic acid group". However, the claim requires that same carboxyl group to be attached to a "cholic acid group" (having 4 carbons) for a total of 5 carbons. One of skill would not have known to label the carboxyl group attached to X1 as the fourth carbon of the "cholic acid group" as claimed. It would have required one of skill in the art undue experimentation to determine the terminal CO₂H group of the cholic acids groups resulted in amide bonds.

Applicants' argue they may be their own lexicographer and define a "cholic acid group" as a cholic acid without the terminal CO₂H (pg 14 of response). Applicants' argument is not persuasive. The specification does not define a "cholic acid group" at all. The specification does

not define a "cholic acid group" as a cholic acid without the terminal CO₂H, or in the instant case, as a substitution resulting in an amide bond.

Applicants argue the species of Impurity II is adequate to represent the genus claimed (pg 16, Section D and Section F). Applicants' argument is not persuasive. Even if the structure of Impurity II was enabled, the structure of Impurity II is not enabling for all compounds having Formula I as claimed which encompasses numerous combinations of X₁, X₂ and X₃. These structures are significantly different and may have different functions than Impurity II. Therefore, Impurity II is not adequate to enable the genus claimed. The specification does not teach any compounds having a deoxycholic acid group, a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group. The mere listing of possible other compounds used as X₁, X₂ and X₃ is not an enabling disclosure; as it would require one of skill undue experimentation to determine how to make or use other compounds within the genus. Thus, the specification does not enable making or using the compounds within the genus claimed.

Applicants argue pg 3, lines 15-21, state the compounds may have a deoxycholic acid group, a hexose monosaccharide group, a pentose-pentose disaccharide group, a hexose-hexose disaccharide group, a pentose-hexose disaccharide group, or a hexose-pentose disaccharide group. Applicants argue one species is disclosed. Therefore, applicants argue the specification enables the genus. Applicants' argument is not persuasive. The specification does not enable one of skill to determine the structure of Impurity II for reasons cited above; therefore, the specification does not enable one species of the genus. Assuming the specification did enable one of skill to determine the structure of Impurity II for argument's sake, applicants' argument would not be persuasive. Applicants do not provide any means of altering or isolating

compounds having such components. Pg 3, lines 15-21, is merely an invitation for further experimentation, which would be undue for one of skill in the art.

3. Claims 41-53 remain rejected as being indefinite because the structures encompassed by the claims are unclear for reasons of record.

The claims require a compound having Formula I having a carboxyl group attached to X1, wherein X1 is cholic or deoxycholic acid (which has a pentose ring plus four carbons). However, Impurity II has a carboxyl group attached to a pentose ring plus three carbons. Impurity II has three carbons between the carboxyl group and the pentose ring instead of four, which would occur if cholic acid were attached to the carboxyl group as claimed. Therefore, it is unclear whether applicants intend the claim to encompass attaching three or four carbons between the carboxyl group and the pentose ring. The limitation of attaching cholic or deoxycholic acid to X2 or X3 is rejected for the same reasons.

Applicants' logic in numbering the carbons of the "cholic acid group" (pg 11) does not correlate to the claims. Carbon number 4 is labeled a carboxyl group, which applicants argue is part of the "cholic acid group". However, the claim requires that same carboxyl group to be attached to a "cholic acid group" (having 4 carbons) for a total of 5 carbons. One of skill would not have known to label the carboxyl group attached to X1 as the fourth carbon of the "cholic acid group" as claimed.

Double Patenting

The rejection of claims 44-53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 09/112074, now US Patent 6,392,069, has been withdrawn because of the terminal disclaimer filed 10-25-02.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson



**MICHAEL WILSON
PRIMARY EXAMINER**